

SEQUENCE LISTING

<110> Yan, Rigiang Tomasselli, Alfredo G. Gurney, Mark E. Emmons, Thomas L. Bienkowski, Mike J. Heinrikson, Robert L. <120> SUBSTRATES AND ASSAYS FOR BETA-SECRETASE ACTIVITY <130> 29915/00281CUS <140> 10/801,509 <141> 2004-03-16 <150> 09/908.943 <151> 2001-07-19 <150> 60/219,795 <151> 2000-07-19 <160> 199 <170> PatentIn Ver. 2.0 <210> 1 <211> 2070 <212> DNA <213> Homo sapiens <400> 1 atggcccaag ccctgccctg gctcctgctg tggatggcg cgggagtgct gcctgcccac 60 ggcacccagc acggcatccg gctgcccctg cgcaqcqqcc tgggggggcgc ccccctgggg 120 gtggagatgg tggacaacct gaggggcaag tcggggcagg gctactacgt ggagatgacc 240 gtgggcagcc ccccgcagac gctcaacatc ctggtggata caggcagcag taactttgca 300 gtgggtgctg cccccaccc cttcctgcat cgctactacc agaggcagct gtccagcaca 360 taccgggacc tccggaaggg tgtgtatgtg ccctacaccc agggcaagtg ggaaggggag 420 ctgggcaccg acctggtaag catccccat ggccccaacg tcactgtgcg tgccaacatt 480 gctgccatca ctgaatcaga caagttcttc atcaacggct ccaactggga aggcatcctg 540 gggctggcct atgctgagat tgccaggcct gacgactccc tggagccttt ctttgactct 600 ctggtaaagc agaccacgt tcccaacctc ttctccctgc acctttgtgg tgctggcttc 660 cccctcaacc agtctgaagt gctggcctct gtcggaggga gcatgatcat tggaggtatc 720 gaccactcgc tgtacacagg cagtctctgg tatacaccca tccggcggga gtggtattat 780 gaggtcatca ttgtgcgggt ggagatcaat ggacaggatc tgaaaatgga ctgcaaggag 840 tacaactatg acaagagcat tgtggacagt ggcaccacca accttcgttt gcccaagaaa 900 gtgtttgaag ctgcagtcaa atccatcaag gcagcctcct ccacggagaa gttccctgat 960 ggtttctggc taggagagca gctggtgtgc tggcaagcag gcaccacccc ttggaacatt 1020 ttcccagtca tctcactcta cctaatqqqt qaqqttacca accagtcctt ccgcatcacc 1080 atcetteege ageaatacet geggeeagtg gaagatgtgg ceaegteeca agacgaetgt 1140 tacaagtttg ccatctcaca gtcatccacg ggcactgtta tgggagctgt tatcatggag 1200 ggcttctacg ttgtctttga tcgggcccga aaacgaattg gctttgctgt cagcgcttgc 1260 catgtgcacg atgagttcag gacggcagcg gtggaaggcc cttttgtcac cttggacatg 1320 gaagactgtg gctacaacat tccacaqaca qatqaqtcaa ccctcatqac cataqcctat 1380 gtcatggctg ccatctgcgc cctcttcatg ctgccactct gcctcatggt gtgtcagtgg 1440 cgctgcctcc gctgcctgcg ccagcagcat gatgactttg ctgatgacat ctccctgctg 1500 aagtgaggag gcccatgggc agaagataga gattcccctg gaccacacct ccgtggttca 1560 ctttggtcac aagtaggaga cacagatggc acctgtggcc agagcacctc aggaccctcc 1620 ccaccacca aatgcctctg ccttgatgga gaaggaaaag gctggcaagg tgggttccag 1680 ggactgtacc tgtaggaaac agaaagaga agaaagaagc actctgctgg cgggaatact 1740 cttggtcacc tcaaatttaa gtcgggaaat tctgctgctt gaaacttcag ccctgaacct 1800

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Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp 35 40 45

Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
50 55 60

Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr 65 70 75 80

Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser 85 90 95

Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr 100 105 110

Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val 115 120 125

Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp 130 135 140

Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile 145 150 155 160

Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
165 170 175

Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp 180 185 190

Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro 195 200 205

Asn Leu Phe Ser Leu His Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln 210 215 220

Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile 225 230 235 240

Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg 245 250 255

Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
260 265 270

Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu 425 Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala 455 Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp 485 Ile Ser Leu Leu Lys 500 <210> 3 <211> 1977

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Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
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Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr 100 105 110

Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val 115 120 125

Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp 130 135 140

Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile 145 150 155 160

Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp 165 170 175

Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Leu Cys Gly

Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly 200 Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu 215 Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser 315 Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile 325 330 Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu 385 390 395 Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala Ile Cys Ala Leu Phe Met Leu Pro Leu 440 Cys Leu Met Val Cys Gln Trp Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp Ile Ser Leu Leu Lys 470

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<212> PRT

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<400> 6
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                                      10
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<212> PRT
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<210> 8
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Glu Ala Asn Tyr Glu Val Glu Phe
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Gly Val Leu Leu Ala Ala Gly Trp
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Ile Ile Lys Met Asp Asn Phe Gly
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Thr His Gly Phe Gln Leu Xaa His
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Cys Tyr Thr His Ser Phe Ser Pro
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      peptide sequence
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<223> Xaa= any amino acid
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<223> Xaa= any amino acid
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<210> 16
<211> 8
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<223> Xaa= any amino acid
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<223> Xaa=any amino acid
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<400> 22
Gly Ser Glu Ser Met Asp Ser Gly Ile Ser Leu Asp Asn Lys Trp
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<211> 17
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Trp Lys Lys Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Lys
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Lys
<210> 24
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Ala Asn Leu Ser Thr Phe Ala Gln Pro Arg Arg
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Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu Val
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Phe Phe Ala Glu
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<211> 16
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 1
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<210> 27
<211> 30
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<400> 27

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Leu Val Xaa Gly Glu Arg Gly Phe Phe Tyr Thr Pro Lys Ala
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Glu Asn Tyr Xaa Asn
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                                      10
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Leu His Ala Leu Gly Gly Cys
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Leu His Ala Leu Gly Gly Cys
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<210> 33
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Cys Gly Glu Arg Gly Phe Phe Tyr
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<211> 5
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  1
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                  5
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<210> 45
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<400> 45
Asp Ala Ala His Pro Gly
<210> 46
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      peptide sequence
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Lys Val Glu Ala Asn Leu Ala Val Glu Gly Glu Arg Lys Lys
                  5
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Lys Val Glu Ala Leu Tyr Ala Val Glu Gly Glu Arg Lys Lys
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<223> Xaa = E, G, I, D, T, cysteic acid or S
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Xaa Ala Asn Tyr Glu Val Glu Phe
<210> 50
<211> 8
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     peptide sequence
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<221> SITE
<222> (2)
<223> Xaa= A, V, I, S, H, Y, T or F
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Glu Xaa Asn Tyr Glu Val Glu Phe
<210> 51
<211> 8
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<223> Description of Artificial Sequence: synthetic
      peptide sequence
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<221> SITE
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<223> Xaa= N, L, K, S, G, T, D, A, Q, or E
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<210> 52
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     peptide sequence
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<223> Xaa= Y, L, M, Nle, F or H
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<223> Xaa= F, W, G, A, H, P, G, N or S
<400> 112
Xaa Phe Ala Xaa Xaa Xaa Xaa
  1
                 5
<210> 113
<211> 9
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 113
Glu Val Asn Leu Asp Ala Glu Phe Arg
<210> 114
<211> 7
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 114
Asp Tyr Lys Asp Asp Lys
<210> 115
<211> 17
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 115
Ala Cys Gly Ser Glu Ser Met Asp Ser Gly Ile Ser Leu Asp Asn Lys
                  5
                                     10
Trp
<210> 116
<211> 17
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
```

```
<400> 116
Trp Lys Lys Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Lys
Lys
<210> 117
<211> 11
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 117
Ala Asn Leu Ser Thr Phe Ala Gln Pro Arg Arg
           5
<210> 118
<211> 22
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 118
Tyr Arg Tyr Gln Ser His Asp Tyr Ala Phe Ser Ser Val Glu Lys Leu
Leu His Leu Gly Gly Cys
             20
<210> 119
<211> 22
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 119
Tyr Arg Tyr Gln Ser His Asp Tyr Ala Phe Ser Ser Val Glu Lys Leu
Leu His Leu Gly Gly Cys
             20
<210> 120
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
```

<223> Description of Artificial Sequence: synthetic

peptide sequence <400> 120 Lys Thr Ile Thr Leu Glu Val Glu Pro Ser 5 <210> 121 <211> 12

- <212> PRT
- <213> Artificial Sequence
- <220>
- <223> Description of Artificial Sequence: synthetic peptide sequence
- <220>
- <221> SITE
- <222> (9)
- <223> Xaa= cysteic acid
- <400> 121
- Val Glu Ala Leu Tyr Leu Val Cys Xaa Gly Glu Arg 1 5 10
- <210> 122
- <211> 11
- <212> PRT
- <213> Artificial Sequence
- <223> Description of Artificial Sequence: synthetic peptide sequence
- <400> 122
- Val Glu Ala Leu Tyr Leu Val Glu Gly Glu Arg
- <210> 123
- <211> 363
- <212> PRT
- <213> Homo sapiens
- <220>
- <223> galactosyltransferase
- Met Ala Ser Lys Ser Trp Leu Asn Phe Leu Thr Phe Leu Cys Gly Ser
- Ala Ile Gly Phe Leu Leu Cys Ser Gln Leu Phe Ser Ile Leu Leu Gly
- Glu Lys Val Asp Thr Gln Pro Asn Val Leu His Asn Asp Pro His Ala
- Arg His Ser Asp Asp Asn Gly Gln Asn His Leu Glu Gly Gln Met Asn
- Phe Asn Ala Asp Ser Ser Gln His Lys Asp Glu Asn Thr Asp Ile Ala

Glu Asn Leu Tyr Gln Lys Val Arg Ile Leu Cys Trp Val Met Thr Gly Pro Gln Asn Leu Glu Lys Lys Ala Lys His Val Lys Ala Thr Trp Ala Gln Arg Cys Asn Lys Val Leu Phe Met Ser Ser Glu Glu Asn Lys Asp Phe Pro Ala Val Gly Leu Lys Thr Lys Glu Gly Arg Asp Gln Leu Tyr Trp Lys Thr Ile Lys Ala Phe Gln Tyr Val His Glu His Tyr Leu Glu 155 Asp Ala Asp Trp Phe Leu Lys Ala Asp Asp Asp Thr Tyr Val Ile Leu 165 Asp Asn Leu Arg Trp Leu Leu Ser Lys Tyr Asp Pro Glu Glu Pro Ile Tyr Phe Gly Arg Arg Phe Lys Pro Tyr Val Lys Gln Gly Tyr Met Ser Gly Gly Ala Gly Tyr Val Leu Ser Lys Glu Ala Leu Lys Arg Phe Val .Asp Ala Phe Lys Thr Asp Lys Cys Thr His Ser Ser Ser Ile Glu Asp 230 235 Leu Ala Leu Gly Arg Cys Met Glu Ile Met Asn Val Glu Ala Gly Asp 250 Ser Arg Asp Thr Ile Gly Lys Glu Thr Phe His Pro Phe Val. Pro Glu His His Leu Ile Lys Gly Tyr Leu Pro Arg Thr Phe Trp Tyr Trp Asn Tyr Asn Tyr Tyr Pro Pro Val Glu Gly Pro Gly Cys Cys Ser Asp Leu 290 295 300 Ala Val Ser Phe His Tyr Val Asp Ser Thr Thr Met Tyr Glu Leu Glu Tyr Leu Val Tyr His Leu Arg Pro Tyr Gly Tyr Leu Tyr Arg Tyr Gln Pro Thr Leu Pro Glu Arg Ile Leu Lys Glu Ile Ser Gln Ala Asn Lys

<210> 124

<211> 405

<212> PRT

<213> Homo sapiens

<220>

<223> Homo sapiens sialylytransferase 1

Asn Glu Asp Thr Lys Val Lys Leu Gly Asn Pro

<400> 124 Ile His Thr Asn Leu Lys Lys Lys Phe Ser Cys Cys Val Leu Val Phe Leu Leu Phe Ala Val Ile Cys Val Trp Lys Glu Lys Lys Gly Ser Tyr Tyr Asp Ser Phe Lys Leu Gln Thr Lys Glu Phe Gln Val Leu Lys Ser Leu Gly Lys Leu Ala Met Gly Ser Asp Ser Gln Ser Val Ser Ser Ser Ser Thr Gln Asp Pro His Arg Gly Arg Gln Thr Leu Gly Ser Leu Arg Gly Leu Ala Lys Ala Lys Pro Glu Ala Ser Phe Gln Val Trp Asn Lys Asp Ser Ser Ser Lys Asn Leu Ile Pro Arg Leu Gln Lys Ile Trp 105 Lys Asn Tyr Leu Ser Met Asn Lys Tyr Lys Val Ser Tyr Lys Gly Pro 120 Gly Pro Gly Ile Lys Phe Ser Ala Glu Ala Leu Arg Cys His Leu Arg Asp His Val Asn Val Ser Met Val Glu Val Thr Asp Phe Pro Phe Asn Thr Ser Glu Trp Glu Gly Tyr Leu Pro Lys Glu Ser Ile Arg Thr Lys 165 170 Ala Gly Pro Trp Gly Arg Cys Ala Val Val Ser Ser Ala Gly Ser Leu Lys Ser Ser Gln Leu Gly Arg Glu Ile Asp Asp His Asp Ala Val Leu Arg Phe Asn Gly Ala Pro Thr Ala Asn Phe Gln Gln Asp Val Gly Thr 215 Lys Thr Thr Ile Arg Leu Met Asn Ser Gln Leu Val Thr Thr Glu Lys Arg Phe Leu Lys Asp Ser Leu Tyr Asn Glu Gly Ile Leu Ile Val Trp Asp Pro Ser Val Tyr His Ser Asp Ile Pro Lys Trp Tyr Gln Asn Pro Asp Tyr Asn Phe Phe Asn Asn Tyr Lys Thr Tyr Arg Lys Leu His Pro Asn Gln Pro Phe Tyr Ile Leu Lys Pro Gln Met Pro Trp Glu Leu Trp 295 300 Asp Ile Leu Gln Glu Ile Ser Pro Glu Glu Ile Gln Pro Asn Pro Pro Ser Ser Gly Met Leu Gly Ile Ile Het Met Thr Leu Cys Asp Gln

330

Val Asp Ile Tyr Glu Phe Leu Pro Ser Lys Arg Lys Thr Asp Val Cys 340 345 350

Tyr Tyr Tyr Gln Lys Phe Phe Asp Ser Ala Cys Thr Met Gly Ala Tyr 355 360 365

His Pro Leu Leu Tyr Glu Lys Asn Leu Val Lys His Leu Asn Gln Gly 370 375 380

Thr Asp Glu Asp Ile Tyr Leu Leu Gly Lys Ala Thr Leu Pro Gly Phe 385 390 395 400

Arg Thr Ile His Cys

<210> 125

<211> 518

<212> PRT

<213> Homo sapiens

<220>

<223> Homo sapiens aspartyl protease 1

<400> 125

Met Gly Ala Leu Ala Arg Ala Leu Leu Leu Pro Leu Leu Ala Gln Trp .1 5 10 15

Leu Leu Arg Ala Ala Pro Glu Leu Ala Pro Ala Pro Phe Thr Leu Pro
20 25 30

Leu Arg Val Ala Ala Ala Thr Asn Arg Val Val Ala Pro Thr Pro Gly 35 40 45

Pro Gly Thr Pro Ala Glu Arg His Ala Asp Gly Leu Ala Leu 50 55 60

Glu Pro Ala Leu Ala Ser Pro Ala Gly Ala Ala Asn Phe Leu Ala Met 65 70 75 80

Val Asp Asn Leu Gln Gly Asp Ser Gly Arg Gly Tyr Tyr Leu Glu Met 85 90 95

18.0

Leu Ile Gly Thr Pro Pro Gln Lys Leu Gln Ile Leu Val Asp Thr Gly
100 105 110

Ser Ser Asn Phe Ala Val Ala Gly Thr Pro His Ser Tyr Ile Asp Thr 115 120 125

Tyr Phe Asp Thr Glu Arg Ser Ser Thr Tyr Arg Ser Lys Gly Phe Asp 130 135 140

Val Thr Val Lys Tyr Thr Gln Gly Ser Trp Thr Gly Phe Val Gly Glu 145 150 155 160

Asp Leu Val Thr Ile Pro Lys Gly Phe Asn Thr Ser Phe Leu Val Asn 165 170 175

Ile Ala Thr Ile Phe Glu Ser Glu Asn Phe Phe Leu Pro Gly Ile Lys

Trp Asn Gly Ile Leu Gly Leu Ala Tyr Ala Thr Leu Ala Lys Pro Ser 195 200 205 Ser Ser Leu Glu Thr Phe Phe Asp Ser Leu Val Thr Gln Ala Asn Ile Pro Asn Val Phe Ser Met Gln Met Cys Gly Ala Gly Leu Pro Val Ala Gly Ser Gly Thr Asn Gly Gly Ser Leu Val Leu Gly Gly Ile Glu Pro Ser Leu Tyr Lys Gly Asp Ile Trp Tyr Thr Pro Ile Lys Glu Glu Trp Tyr Tyr Gln Ile Glu Ile Leu Lys Leu Glu Ile Gly Gln Ser Leu Asn Leu Asp Cys Arg Glu Tyr Asn Ala Asp Lys Ala Ile Val Asp Ser Gly Thr Thr Leu Leu Arg Leu Pro Gln Lys Val Phe Asp Ala Val Val Glu Ala Val Ala Arg Ala Ser Leu Ile Pro Glu Phe Ser Asp Gly Phe 330 Trp Thr Gly Ser Gln Leu Ala Cys Trp Thr Asn Ser Glu Thr Pro Trp Ser Tyr Phe Pro Lys Ile Ser Ile Tyr Leu Arg Asp Glu Asn Ser Ser Arg Ser Phe Arg Ile Thr Ile Leu Pro Gln Leu Tyr Ile Gln Pro Met 375 Met Gly Ala Gly Leu Asn Tyr Glu Cys Tyr Arg Phe Gly Ile Ser Pro Ser Thr Asn Ala Leu Val Ile Gly Ala Thr Val Met Glu Gly Phe Tyr Val Ile Phe Asp Arg Ala Gln Lys Arg Val Gly Phe Ala Ala Ser Pro Cys Ala Glu Ile Ala Gly Ala Ala Val Ser Glu Ile Ser Gly Pro Phe Ser Thr Glu Asp Val Ala Ser Asn Cys Val Pro Ala Gln Ser Leu Ser Glu Pro Ile Leu Trp Ile Val Ser Tyr Ala Leu Met Ser Val Cys Gly 470 Ala Ile Leu Leu Val Leu Ile Val Leu Leu Leu Pro Phe Arg Cys 490 Gln Arg Arg Pro Arg Asp Pro Glu Val Val Asn Asp Glu Ser Ser Leu 500 505 Val Arg His Arg Trp Lys

<210> 126

. . .

```
<211> 255
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<212> PRT

<213> Homo sapiens

<220>

<223> Homo sapiens syntaxin 6

<400> 126

Met Ser Met Glu Asp Pro Phe Phe Val Val Lys Gly Glu Val Gln Lys

1 10 15

Ala Val Asn Thr Ala Gln Gly Leu Phe Gln Arg Trp Thr Glu Leu Leu 20 25 30

Gln Asp Pro Ser Thr Ala Thr Arg Glu Glu Ile Asp Trp Thr Thr Asn $35 \hspace{1cm} 40 \hspace{1cm} 45$

Glu Leu Arg Asn Asn Leu Arg Ser Ile Glu Trp Asp Leu Glu Asp Leu
50 55 60

Asp Glu Thr Ile Ser Ile Val Glu Ala Asn Pro Arg Lys Phe Asn Leu 65 70 75 80

Asp Ala Thr Glu Leu Ser Ile Arg Lys Ala Phe Ile Thr Ser Thr Arg 85 90 95

Gln Val Val Arg Asp Met Lys Asp Gln Met Ser Thr Ser Ser Val Gln 100 105 110

Ala Leu Ala Glu Arg Lys Asn Arg Gln Ala Leu Leu Gly Asp Ser Gly
115 120 125

Ser Gln Asn Trp Ser Thr Gly Thr Thr Asp Lys Tyr Gly Arg Leu Asp 130 135 140

Arg Glu Leu Gln Arg Ala Asn Ser His Phe Ile Glu Glu Gln Gln Ala 145 150 155 160

Gln Gln Gln Leu Ile Val Glu Gln Gln Asp Glu Gln Leu Glu Leu Val 165 170 : 175

Ser Gly Ser Ile Gly Val Leu Lys Asn Met Ser Gln Arg Ile Gly Gly
180 185 190

Glu Leu Glu Glu Gln Ala Val Met Leu Glu Asp Phe Ser His Glu Leu 195 200 205

Glu Ser Thr Gln Ser Arg Leu Asp Asn Val Met Lys Lys Leu Ala Lys 210 215 220

Val Ser His Met Thr Ser Asp Arg Gln Trp Cys Ala Ile Ala Ile 225 230 235 240

Leu Phe Ala Val Leu Leu Val Val Leu Ile Leu Phe Leu Val Leu 245 250 255

<210> 127

<211> 1728

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: nucleic acid encoding recombinant fusion protein

```
<400> 127
atgctgctgc tgctgctgct gctgggcctg aggctacagc tctccctggg catcatccca 60
gttgaggagg agaacccgga cttctggaac cgcgaggcag ccgaggccct gggtgccgcc 120
 aagaagetge ageetgeaca gacageegee aagaacetea teatetteet gggegatggg 180
atgggggtgt ctacggtgac agctgccagg atcctaaaag ggcagaagaa ggacaaactg 240
gggcctgaga tacccctggc catggaccgc ttcccatatg tggctctgtc caagacatac 300
 aatgtagaca aacatgtgcc agacagtgga gccacagcca cggcctacct gtgcggggtc 360
 aagggcaact tecagaccat tggettgagt geageegeee getttaacca gtgcaacaeg 420
 acacgcggca acgaggtcat ctccgtgatg aatcgggcca agaaagcagg gaagtcagtg 480
ggagtggtaa ccaccacacg agtgcagcac gcctcgccag ccggcaccta cgcccacacg 540
gtgaaccgca actggtactc ggacgccgac gtgcctgcct cggcccgcca ggaggggtgc 600
 caggacatcg ctacgcagct catctccaac atggacattg acgtgatcct aggtggaggc 660
 cgaaagtaca tgtttcccat gggaacccca gaccctgagt acccagatga ctacagccaa 720
ggtgggacca ggctggacgg gaagaatctg gtgcaggaat ggctggcgaa gcgccagggt 780
gcccggtatg tgtggaaccg cactgagctc atgcaggctt ccctggaccc gtctgtgacc 840
 catctcatgg gtctctttga gcctggagac atgaaatacg agatccaccg agactccaca 900
 ctggacccct ccctgatgga gatgacagag gctgccctgc gcctgctgag caggaacccc 960
 cgcggcttct tcctcttcgt ggagggtggt cgcatcgacc atggtcatca tgaaagcagg 1020
 gcttaccggg cactgactga gacgatcatg ttcgacgacg ccattgagag ggcgggccag 1080
ctcaccagcg aggaggacac gctgagcctc gtcactgccg accactccca cgtcttctcc 1140 ttcggaggct acccctgcg agggagctcc atcttcgggc tggcccctgg caaggcccgg 1200
gacaggaagg cctacacggt cctcctatac ggaaacggtc caggctatgt gctcaaggac 1260
ggcgcccggc cggatgttac cgagagcgag agcgggagcc ccgagtatcg gcagcagtca 1320
gcagtgcccc tggacgaaga gacccacgca ggcgaggacg tggcggtgtt cgcgcgcggc 1380
 ccgcaggcgc acctggttca cggcgtgcag gagcagacct tcatagcgca cgtcatggcc 1440
 ttcgccgcct gcctggagcc ctacaccgcc tgcgacctgg cgcccccgc cggcaccacc 1500
 gacgccgcgc acccaggtaa ctatgaagtt gaattccgaa gagcactcta cgtagagggt 1560
 gaaagaggat tettetacae teeaaaggea etetaceteg tagagggtga aagaggatte 1620
 ttctacacta gtctcatgac catagcctat gtcatggctg ccatctgcgc cctcttcatg 1680
 ctgccactct gcctcatggt ggactacaag gatgatgatg acaagtag
 <210> 128
 <211> 575
 <212> PRT
 <213> Artificial Sequence
 <223> Description of Artificial Sequence: recombinant
       fusion protein sequence
 <400> 128
 Met Leu Leu Leu Leu Leu Gly Leu Arg Leu Gln Leu Ser Leu
 Gly Ile Ile Pro Val Glu Glu Glu Asn Pro Asp Phe Trp Asn Arg Glu .
Ala Ala Glu Ala Leu Gly Ala Ala Lys Lys Leu Gln Pro Ala Gln Thr
. Ala Ala Lys Asn Leu Ile Ile Phe Leu Gly Asp Gly Met Gly Val Ser
 Thr Val Thr Ala Ala Arg Ile Leu Lys Gly Gln Lys Lys Asp Lys Leu
 Gly Pro Glu Ile Pro Leu Ala Met Asp Arg Phe Pro Tyr Val Ala Leu
```

Ser Lys Thr Tyr Asn Val Asp Lys His Val Pro Asp Ser Gly Ala Thr

105

110

100

Ala Thr Ala Tyr Leu Cys Gly Val Lys Gly Asn Phe Gln Thr Ile Gly 120 Leu Ser Ala Ala Ala Arg Phe Asn Gln Cys Asn Thr Thr Arg Gly Asn 135 Glu Val Ile Ser Val Met Asn Arg Ala Lys Lys Ala Gly Lys Ser Val Gly Val Val Thr Thr Arg Val Gln His Ala Ser Pro Ala Gly Thr Tyr Ala His Thr Val Asn Arg Asn Trp Tyr Ser Asp Ala Asp Val Pro Ala Ser Ala Arg Gln Glu Gly Cys Gln Asp Ile Ala Thr Gln Leu Ile Ser Asn Met Asp Ile Asp Val Ile Leu Gly Gly Gly Arg Lys Tyr Met Phe Pro Met Gly Thr Pro Asp Pro Glu Tyr Pro Asp Asp Tyr Ser Gln 230... Gly Gly Thr Arg Leu Asp Gly Lys Asn Leu Val Gln Glu Trp Leu Ala 250 Lys Arg Gln Gly Ala Arg Tyr Val Trp Asn Arg Thr Glu Leu Met Gln 265 Ala Ser Leu Asp Pro Ser Val Thr His Leu Met Gly Leu Phe Glu Pro Gly Asp Met Lys Tyr Glu Ile His Arg Asp Ser Thr Leu Asp Pro Ser Leu Met Glu Met Thr Glu Ala Ala Leu Arg Leu Leu Ser Arg Asn Pro Arg Gly Phe Phe Leu Phe Val Glu Gly Gly Arg Ile Asp His Gly His His Glu Ser Arg Ala Tyr Arg Ala Leu Thr Glu Thr Ile Met Phe Asp Asp Ala Ile Glu Arg Ala Gly Gln Leu Thr Ser Glu Glu Asp Thr Leu Ser Leu Val Thr Ala Asp His Ser His Val Phe Ser Phe Gly Gly Tyr Pro Leu Arg Gly Ser Ser Ile Phe Gly Leu Ala Pro Gly Lys Ala Arg 390 Asp Arg Lys Ala Tyr Thr Val Leu Leu Tyr Gly Asn Gly Pro Gly Tyr Val Leu Lys Asp Gly Ala Arg Pro Asp Val Thr Glu Ser Glu Ser Gly

```
Ser Pro Glu Tyr Arg Gln Gln Ser Ala Val Pro Leu Asp Glu Glu Thr
His Ala Gly Glu Asp Val Ala Val Phe Ala Arg Gly Pro Gln Ala His
Leu Val His Gly Val Gln Glu Gln Thr Phe Ile Ala His Val Met Ala
Phe Ala Ala Cys Leu Glu Pro Tyr Thr Ala Cys Asp Leu Ala Pro Pro
Ala Gly Thr Thr Asp Ala Ala His Pro Gly Asn Tyr Glu Val Glu Pro
Arg Arg Ala Leu Tyr Val Glu Gly Glu Arg Gly Phe Phe Tyr Thr Pro
Lys Ala Leu Tyr Leu Val Glu Gly Glu Arg Gly Phe Phe Tyr Thr Ser
Leu Met Thr Ile Ala Tyr Val Met Ala Ala Ile Cys Ala Leu Phe Met
Leu Pro Leu Cys Leu Met Val Asp Tyr Lys Asp Asp Asp Lys
                                    570
                                                         575
<210> 129
<211> 5
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 129
Lys Met Asp Ala Glu
 1
<210> 130
<211> 5
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 130
Gly Arg Arg Gly Ser
<210> 131
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
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<223> Description of Artificial Sequence: synthetic

peptide sequence

```
<400> 131
Val Glu Ala Asn Tyr Glu Val Glu Gly Glu
                  5
<210> 132
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
Val Glu Ala Asn Tyr Ala Val Glu Gly Glu
<210> 133
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 133
Lys Thr Ile Asn Leu Glu Val Glu Pro Ser
                  5
<210> 134
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<220>
<221> MOD RES
<222> (5)
<223> Nle
<400> 134
Lys Thr Ile Asn Xaa Glu Val Glu Pro Ser
            5
<210> 135
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<221> MOD_RES
```

```
<222> (5)
<223> Nle
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 135
Lys Thr Ile Asn Xaa Glu Val Asp Pro Ser
                  5
<210> 136
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<221> MOD RES
<222> (5)
<223> Nle
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 136
Lys Thr Ile Asn Xaa Asp Val Asp Pro Ser
                  5
<210> 137
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 137
Lys Thr Ile Ser Leu Asp Val Glu Pro Ser
                  5
                                     10
<210> 138
<211> 10
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 138
Lys Thr Ile Ser Leu Asp Val Asp Pro Ser
                  5
 1
                                      10
<210> 139
<211> 4
<212> PRT
<213> Artificial Sequence
```

```
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 139
Lys Met Asp Ala
 1
<210> 140
<211> 4
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 140
Ser Tyr Glu Val
 1
<210> 141
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 141
Ser Glu Val Ser Tyr Glu Val Glu Phe Arg
<210> 142
<211> 4
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 142
Asn Leu Asp Ala
 1
<210> 143
<211> 10
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 143
Ser Glu Val Ser Tyr Asp Ala Glu Phe Arg
```

```
<210> 144
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 144
Ser Glu Val Ser Tyr Glu Ala Glu Phe Arg
<210> 145
<211> 25
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 145
Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser
Glu Val Ser Tyr Glu Val Glu Phe Arg
             20
<210> 146
<211> 20
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 146
Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Ser Tyr Glu
Val Glu Phe Arg
             20
<210> 147
<211> 15
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 147
Lys Thr Glu Glu Ile Ser Glu Val Ser Tyr Glu Val Glu Phe Arg
                                      10
```

```
<210> 148
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 148
Thr Glu Val Ser Tyr Glu Val Glu Phe Arg
                  5
<210> 149
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 149
Ser Glu Val Asp Tyr Glu Val Glu Phe Arg
                  5
  1
<210> 150
<211> 10
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 150
Thr Glu Val Asp Tyr Glu Val Glu Phe Arg.
  1
                  5
<210> 151
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 151
Thr Glu Ile Asp Tyr Glu Val Glu Phe Arg
                  5
<210> 152
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
```

```
peptide sequence
<400> 152
Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg
<210> 153
<211> 10
```

<212> PRT <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: synthetic peptide sequence

<400> 153 Ser Glu Ile Asp Tyr Glu Val Glu Phe Arg

<210> 154 <211> 13 <212> PRT <213> Artificial Sequence

<220> <221> SITE <222> (11)

<223> Xaa=tryptophan

<223> Description of Artificial Sequence: synthetic peptide sequence

<400> 154 Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys

<210> 155 <211> 18 <212> PRT <213> Artificial Sequence

<220> <221> SITE <222> (16)

<223> Xaa=tryptophan

<223> Description of Artificial Sequence: synthetic peptide sequence

Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa 10 15

Lys Lys

<210> 156 <211> 23

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<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (21)
<223> Xaa=tryptophan
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 156
Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr Glu Val
Glu Phe Arg Xaa Lys Lys
       20
<210> 157
<211> 28
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<220>
<221> SITE
<222> (26)
<223> Xaa=tryptophan
<400> 157
Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser
                                     10
Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
                                  25
<210> 158
<211> 13
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (11)
<223> Xaa=tryptophan
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
<210> 159
<211> 18
```

```
<212> PRT
 <213> Artificial Sequence
 <220>
 <223> Description of Artificial Sequence: synthetic
       peptide sequence
 <220>
 <221> SITE
 <222> (16)
 <223> Xaa=tryptophan
 <400> 159
Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg
 Xaa Lys Lys
 <210> 160
 <211> 23
 <212> PRT
 <213> Artificial Sequence
 <220>
 <221> SITE
 <222> (21)
 <223> Xaa=tryptophan
 <223> Description of Artificial Sequence: synthetic
       peptide
 <400> 160
 Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr
                                       10
 Glu Val Glu Phe Arg Xaa Lys Lys
                 20
 <210> 161
 <211> 28
 <212> PRT
 <213> Artificial Sequence
 <220>
 <221> SITE
 <222> (26)
 <223> Xaa=tryptophan
 <220>
 <223> Description of Artificial Sequence: synthetic
       peptide sequence
 <400> 161
 Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile
 Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
```

```
<210> 162
<211> 13
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (11)
<223> Xaa=oregon green
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 162
Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
<210> 163
<211> 18
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (16)
<223> Xaa=oregon green
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 163
Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa
                                      10
Lys Lys
<210> 164
<211> 23
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (21)
<223> Xaa=oregon green
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 164
Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr Glu
                                      10
Val Glu Phe Arg Xaa Lys Lys
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20

```
<210> 165
<211> 28
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (26)
<223> Xaa=oregon green
<223> Description of Artificial Sequence: synthetic peptide sequence
<400> 165
Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser
                                      10
Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
<210> 166
<211> 13
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (11)
<223> Xaa=oregon green
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 166
Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
                  5
<210> 167
<211> 18
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (16)
<223> Xaa=oregon green
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400 > 167
Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg
                  5
                                      10
```

Xaa Lys Lys

```
<210> 168
<211> 23
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (21)
<223> Xaa=oregon green
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 168
Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr
                                                           15
Glu Val Glu Phe Arg Xaa Lys Lys
                20
<210> 169
<211> 28
<212> PRT
<213> Artificial Sequence
<220>
<221> SITE
<222> (26)
<223> Xaa=oregon green
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 169
Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile
Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Xaa Lys Lys
                20
<210> 170
<211> 10
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
      peptide sequence
Ser Glu Val Asn Tyr Glu Val Glu Phe Arg
  1
                                      10
<210> 171
<211> 47
<212> DNA
<213> Artificial Sequence
```

```
<220>
<223> Description of Artificial Sequence: synthetic
      primer for site-directed mutagenesis of APP
<400> 171
gagatetetg aaattagtta tgaagtagaa tteegacatg acteagg
                                                                    47
<210> 172
<211> 48
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      primer for site-directed mutagenesis of APP
tgagtcatgt cggaattcta cttcataact aatttcagag atctcctc
                                                                    48
<210> 173
<211> 47
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      primer for site-directed mutagenesis of APP
<400> 173
gagatetetg aaagtagtta tgaagtagaa tteegacatg acteagg
                                                                    47
<210> 174
<211> 48
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      primer for site-directed mutagenesis of APP
<400> 174
tgagtcatgt cggaattcta cttcataact actttcagag atctcctc
                                                                    48
<210> 175
<211> 47
<212> DNA
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
      primer for site-directed mutagenesis of APP
gagatetetg aaattagtta tgaagcagaa tteegacatg acteagg
                                                                    47
<210> 176
<211> 48
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      primer for site-directed mutagenesis of APP
```

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<400> 176
tgagtcatgt cggaattctg cttcataact aatttcagag atctcctc
<210> 177
<211> 5
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 177
Val Ser Tyr Glu Val
<210> 178
<211> 5
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 178
Val Ser Tyr Asp Ala
1
<210> 179
<211> 5
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 179
Ile Ser Tyr Glu Val
  1
                  5
<210> 180
<211> 5
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 180
Val Lys Met Asp Ala
  1
<210> 181
<211> 47
<212> DNA
<213> Artificial Sequence
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48

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<220>
<223> Description of Artificial Sequence: synthetic
     primer for generating mutant construct named
      MBPC125-SYEV
<400> 181
                                                                   47
gacatctctg aagtgagtta ttaggcagaa ttccgacatg actcagg
<210> 182
<211> 48
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      primer for generating mutant construct named
      MBPC125-SYEV
tgagtcatgt cggaattctg cctaataact cacttcagag atctcctc
                                                                   48
<210> 183
<211> 6
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 183
Lys Lys Ser Tyr Glu Val
<210> 184
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 184
Val Glu Ala Asn Tyr Glu Val Glu Gly Glu
<210> 185
<211> 10
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
Val Glu Ala Asn Tyr Ala Val Glu Gly Glu
```

5

```
<210> 186
<211> 8
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 186
Asp Tyr Lys Asp Asp Asp Lys
<210> 187
<211> 4
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
      peptide sequence
<400> 187
Ser Tyr Glu Ala
 1
<210> 188
<211> 4
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 188
Ser Tyr Ala Val
 1
<210> 189
<211> 5
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: synthetic
     peptide sequence
<400> 189
Val Ser Tyr Glu Ala
<210> 190
<211> 13
<212> PRT
<213> Artificial sequence
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<220>
<223> Description of artificial sequence: synthetic peptide sequence
<400> 190
Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Trp Lys Lys
<210> 191
<211> 23
<212> PRT
<213> Artificial sequence
<220>
<223> Description of artificial sequence: synthetic peptide sequence
<400> 191
Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr Glu
Val Glu Phe Arg Trp Lys Lys
<210> 192
<211> 15
<212> PRT
<213> Artificial sequence
<220>
<223> Description of artificial sequence: synthetic peptide sequence
<220>
<221> SITE
<222> (1)..(1)
<223> amino acid at position 1 is biotinylated
<220>
<221> SITE
<222> (14)..(14)
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<223> cys at position 14 is derivatized with an oregon green

<400> 192 Lys Glu Ile Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Lys <210> 193 <211> 22 <212> PRT <213> Artificial sequence <220> <223> Description of artificial sequence: synthetic peptide sequence <220> <221> SITE <222> (1)..(1) <223> amino acid at position 1 is biotinylated <220> <221> SITE <222> (21)..(21) <223> cys at position 21 is derivatized with an oregon green <400> 193 Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Ile Ser Tyr Glu Val Glu Phe Arg Lys Lys 20

<210> 194

<211> 6806

<212> DNA

<213> Artificial sequence

<223> Description of artificial sequence: synthetic DNA sequence <400> 194 ccgacaccat cgaatggcgc aaaacctttc gcggtatggc atgatagcgc ccggaagaga 60 gtcaattcag ggtggtgaat gtgaaaccag taacgttata cgatgtcgca gagtatgccg 120 gtgtctctta tcagaccgtt tcccgcgtgg tgaaccaggc cagccacgtt tctgcgaaaa 180 cgcgggaaaa agtggaagcg gcgatggcgg agctgaatta cattcccaac cgcgtggcac 240 aacaactggc gggcaaacag tcgttgctga ttggcgttgc cacctccagt ctggccctgc 300 acgcgccgtc gcaaattgtc gcggcgatta aatctcgcgc cgatcaactg ggtgccagcg 360 tggtggtgtc gatggtagaa cgaagcggcg tcgaagcctg taaagcggcg gtgcacaatc 420 ttctcgcgca acgcgtcagt gggctgatca ttaactatcc gctggatgac caggatgcca 480 ttgctgtgga agctgcctgc actaatgttc cggcgttatt tcttgatgtc tctgaccaga 540 cacccatcaa cagtattatt ttctcccatg aagacggtac gcgactgggc gtggagcatc 600 tggtcgcatt gggtcaccag caaatcgcgc tgttagcggg cccattaagt tctgtctcgg 660 egegtetgeg tetggetgge tggeataaat ateteaeteg caateaaatt cageegatag 720 cggaacggga aggcgactgg agtgccatgt ccggttttca acaaaccatg caaatgctga 780 atgagggcat cgttcccact gcgatgctgg ttgccaacga tcagatggcg ctgggcgcaa 840. tgcgcgccat taccgagtcc gggctgcgcg ttggtgcgga tatctcggta gtgggatacg 900 acgataccga agacagetea tgttatatee egeegttaae caccateaaa caggatttte 960. gcctgctggg gcaaaccagc gtggaccgct tgctgcaact ctctcagggc caggcggtga 1020 agggcaatca gctgttgccc gtctcactgg tgaaaagaaa aaccaccctg gcgcccaata 1080 cgcaaaccgc ctctccccgc gcgttggccg attcattaat gcagctggca cgacaggttt 1140 1200 ecegactgga aagegggeag tgagegeaac geaattaatg tgagttaget caeteattag gcacaattct catgtttgac agcttatcat cgactgcacg gtgcaccaat gcttctggcg 1260 tcaggcagcc atcggaagct gtggtatggc tgtgcaggtc gtaaatcact gcataattcg 1320 tgtcgctcaa ggcgcactcc cgttctggat aatgtttttt gcgccgacat cataacggtt 1380 ctggcaaata ttctgaaatg agctgttgac aattaatcat cggctcgtat aatgtgtgga 1440 1500 attgtgagcg gataacaatt tcacacagga aacagccagt ccgtttaggt gttttcacga gcacttcacc aacaaggacc atagattatg aaaactgaag aaggtaaact ggtaatctgg 1560 attaacggcg ataaaggcta taacggtctc gctgaagtcg gtaagaaatt cgagaaagat 1620 accggaatta aagtcaccgt tgagcatccg gataaactgg aagagaaatt cccacaggtt 1680 1740 gcggcaactg gcgatggccc tgacattatc ttctgggcac acgaccgctt tggtggctac

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caacgeggee tttttaeggt teetggeett ttgetggeet tttgeteaca tgttetttee
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tgcgttatcc cctgattctg tggataaccg tattaccgcc tttgagtgag ctgataccgc
                                                                     5820
tegeegeage egaacgaeeg agegeagega gteagtgage gaggaagegg aagagegeet
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gatgcggtat tttctcctta cgcatctgtg cggtatttca caccgcatat ggtgcactct
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                                                                     6720
ggcaaccccg ccagcctagc cgggtcctca acgacaggag cacgatcatg cgcacccgtg
                                                                     6780
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<210> 195
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<220>

<223>.Description of artificial sequence: synthetic peptide sequence

<220>

<221> MOD RES

<222> (1)..(1)

<211> 13

<212> PRT

<213> Artificial sequence

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<223> ACETYLATION (MCA)
 <220>
 <221> SITE
 <222> (11)..(11)
<223> 2,4-dinitrophenyl group after the Lys at position 11
  <400> 195
 Ser Glu Val Asn Leu Asp Ala Glu Phe Arg Lys Arg Arg
  <210> 196
  <211> 12
  <212> PRT
  <213> Artificial sequence
 <220>
<223> Description of artificial sequence: synthetic peptide sequence
  <220>
  <221> SITE
  <222> (4)..(4)
  <223> amino acid at position 4 has been derivatized with a statine
  <400> 196
  Ser Glu Val Asn Val Ala Glu Phe Arg Gly Gly Cys
 <210> 197
  <211> 10
  <212> PRT
  <213> synthetic peptide sequence
  <220>
  <221> SITE
  <222> (4)..(4)
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<223> amino acid at position 4 has been derivatized with a statine

<220>

<221> SITE

<222> (10)..(10)

<223> amino acid at position 10 has been derivatized with Bodipy FL

<400> 197

Ser Glu Val Asn Val Ala Glu Phe Arg Cys 1 5 10

<210> 198

<211> 2043

<212> DNA

<213> Mus musculus

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Glu Glu Ser Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val 50 55 60

Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr 65 70 75 80

Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser 85 90 95

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Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp 465 470 475 480

Arg Cys Leu Arg Cys Leu Arg His Gln His Asp Asp Phe Ala Asp Asp 485 . 490 495

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